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 NEWS  5  NOV 30   PHAR reloaded with additional data
 NEWS  6  DEC 01   LISA now available on STN
 NEWS  7  DEC 09   12 databases to be removed from STN on December 31, 2004
 NEWS  8  DEC 15   MEDLINE update schedule for December 2004
 NEWS  9  DEC 17   ELCOM reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
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                   alerts (SDIs) affected
 NEWS  11 DEC 17   SOLIDSTATE reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  12 DEC 17   CERAB reloaded; updating to resume; current-awareness
                   alerts (SDIs) affected
 NEWS  13 DEC 17   THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB
 NEWS  14 DEC 30   EPFULL: New patent full text database to be available on STN
 NEWS  15 DEC 30   CAPLUS - PATENT COVERAGE EXPANDED
 NEWS  16 JAN 03   No connect-hour charges in EPFULL during January and
                   February 2005
 NEWS  17 FEB 25   CA/CAPLUS - Russian Agency for Patents and Trademarks
                   (ROSPATENT) added to list of core patent offices covered
 NEWS  18 FEB 10   STN Patent Forums to be held in March 2005
 NEWS  19 FEB 16   STN User Update to be held in conjunction with the 229th ACS
                   National Meeting on March 13, 2005
 NEWS  20 FEB 28   PATDPAFULL - New display fields provide for legal status
                   data from INPADOC
 NEWS  21 FEB 28   BABS - Current-awareness alerts (SDIs) available
 NEWS  22 FEB 28   MEDLINE/LMEDLINE reloaded
 NEWS  23 MAR 02   GBFULL: New full-text patent database on STN
 NEWS  24 MAR 03   REGISTRY/ZREGISTRY - Sequence annotations enhanced
 NEWS  25 MAR 03   MEDLINE file segment of TOXCENTER reloaded
 NEWS  26 MAR 22   KOREAPAT now updated monthly; patent information enhanced
 NEWS  27 MAR 22   Original IDE display format returns to REGISTRY/ZREGISTRY
 NEWS  28 MAR 22   PATDPASPC - New patent database available
 NEWS  29 MAR 22   REGISTRY/ZREGISTRY enhanced with experimental property tags

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FILE 'HOME' ENTERED AT 16:47:12 ON 22 MAR 2005

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FULL ESTIMATED COST	0.21	0.21

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FILE 'MEDICONF' ENTERED AT 16:47:45 ON 22 MAR 2005

FILE 'PASCAL' ENTERED AT 16:47:45 ON 22 MAR 2005

=> malaria and (l-arginine or no or s-nitrosothiol)

L1	178	FILE AGRICOLA
L2	880	FILE BIOTECHNO
L3	5	FILE CONFSCI
L4	88	FILE HEALSAFE
L5	0	FILE IMSDRUGCONF
L6	1903	FILE LIFESCI
L7	0	FILE MEDICONF
L8	1907	FILE PASCAL

TOTAL FOR ALL FILES
L9 4961 MALARIA AND (L-ARGININE OR NO OR S-NITROSOTHIOL)

=> malaria and (l-arginine or nitric oxide or s-nitrosothiol)

L10	6	FILE AGRICOLA
L11	82	FILE BIOTECHNO
L12	7	FILE CONFSCI
L13	1	FILE HEALSAFE
L14	0	FILE IMSDRUGCONF

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L15         126 FILE LIFESCI
L16           0 FILE MEDICONF
L17         104 FILE PASCAL

TOTAL FOR ALL FILES
L18         326 MALARIA AND (L-ARGININE OR NITRIC OXIDE OR S-NITROSOTHIOL)

=> malaria and (nitric oxide) and (treatment or inhibiting or inhibition or killing)
L19           2 FILE AGRICOLA
L20          26 FILE BIOTECHNO
L21           1 FILE CONFSCI
L22           0 FILE HEALSAFE
L23           0 FILE IMSDRUGCONF
L24          35 FILE LIFESCI
L25           0 FILE MEDICONF
L26          31 FILE PASCAL

TOTAL FOR ALL FILES
L27          95 MALARIA AND (NITRIC OXIDE) AND (TREATMENT OR INHIBITING OR INHIB
                ITION OR KILLING)

=> 127 and plasmodium
L28           1 FILE AGRICOLA
L29          21 FILE BIOTECHNO
L30           0 FILE CONFSCI
L31           0 FILE HEALSAFE
L32           0 FILE IMSDRUGCONF
L33          29 FILE LIFESCI
L34           0 FILE MEDICONF
L35          26 FILE PASCAL

TOTAL FOR ALL FILES
L36          77 L27 AND PLASMODIUM

=> dup rem
ENTER L# LIST OR (END):136
DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L36
L37           50 DUP REM L36 (27 DUPLICATES REMOVED)

=> 137 and py<1999
L38           1 S L37
L39           0 FILE AGRICOLA
L40          20 S L37
L41          11 FILE BIOTECHNO
L42           0 S L37
'1999' NOT A VALID FIELD CODE
L43           0 FILE CONFSCI
L44           0 S L37
L45           0 FILE HEALSAFE
L46           0 S L37
L47           0 FILE IMSDRUGCONF
L48          16 S L37
L49           7 FILE LIFESCI
L50           0 S L37
'1999' NOT A VALID FIELD CODE
L51           0 FILE MEDICONF
L52          13 S L37

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                                                         ENTRY    SESSION
FULL ESTIMATED COST                                      12.13      12.34

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=> malaria and (nitric oxide) and plasmodium and (treatment or inhibition or killing)
L53           1 FILE AGRICOLA
L54          21 FILE BIOTECHNO
L55           0 FILE CONFSCI
L56           0 FILE HEALSAFE
L57           0 FILE IMSDRUGCONF
L58          29 FILE LIFESCI
L59           0 FILE MEDICONF
L60          26 FILE PASCAL

TOTAL FOR ALL FILES
L61          77 MALARIA AND (NITRIC OXIDE) AND PLASMODIUM AND (TREATMENT OR
                INHIBITION OR KILLING)

=> dup rem
ENTER L# LIST OR (END):l53-158
L55 HAS NO ANSWERS
L56 HAS NO ANSWERS
L57 HAS NO ANSWERS
DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L53
PROCESSING COMPLETED FOR L54
PROCESSING COMPLETED FOR L55
PROCESSING COMPLETED FOR L56
PROCESSING COMPLETED FOR L57
PROCESSING COMPLETED FOR L58
L62           37 DUP REM L53-L58 (14 DUPLICATES REMOVED)

=> d l62 ibib abs total

L62  ANSWER 1 OF 37  LIFESCI     COPYRIGHT 2005 CSA on STN
ACCESSION NUMBER:    2005:16919  LIFESCI
```

TITLE: Suppression of **Plasmodium** chabaudi Parasitemia Is Independent of the Action of Reactive Oxygen Intermediates and/or **Nitric Oxide**
AUTHOR: Gillman, Brad M.; Batchelder, Joan; Flaherty, Patrick; Weidanz, William P.
CORPORATE SOURCE: Department of Medical Microbiology and Immunology, University of Wisconsin Medical School, Madison, Wisconsin
SOURCE: Infection and Immunity [Infect. Immun.], (20041100) vol. 72, no. 11, pp. 6359-6366.
ISSN: 0019-9567.
DOCUMENT TYPE: Journal
FILE SEGMENT: K
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The **killing** of blood-stage **malaria** parasites in vivo has been attributed to reactive intermediates of oxygen (ROI) and of nitrogen (RNI). However, in the case of the latter, this contention is challenged by recent observations that parasitemia was not exacerbated in **nitric oxide** synthase (NOS) knockout (KO) (NOS2 super(-/-) or NOS3 super(-/-)) mice or in mice treated with NOS inhibitors. We now report that the time course shows that **Plasmodium** chabaudi parasitemia in NADPH oxidase KO (p47 super(phox-/-)) mice also was not exacerbated, suggesting a minimal role for ROI-mediated **killing** of blood-stage parasites. It is possible that the production of protective antibodies during **malaria** may mask the function of ROI and/or RNI. However, parasitemia in B-cell-deficient J sub(H) super(-/-) x NOS2 super(-/-) or J sub(H) super(-/-) x p47 super(phox-/-) mice was not exacerbated. In contrast, the magnitude of peak parasitemia was significantly enhanced in p47 super(phox-/-) mice treated with the xanthine oxidase inhibitor allopurinol, but the duration of patent parasitemia was not prolonged. Whereas the time course of parasitemia in NOS2 super(-/-) x p47 super(phox-/-) mice was nearly identical to that seen in normal control mice, allopurinol **treatment** of these double-KO mice also enhanced the magnitude of peak parasitemia. Thus, ROI generated via the xanthine oxidase pathway contribute to the control of ascending P. chabaudi parasitemia during acute **malaria** but alone are insufficient to suppress parasitemia to subpatent levels. Together, these results indicate that ROI or RNI can contribute to, but are not essential for, the suppression of parasitemia during blood-stage **malaria**.

L62 ANSWER 2 OF 37 LIFESCI COPYRIGHT 2005 CSA on STN
ACCESSION NUMBER: 2005:13550 LIFESCI
TITLE: Induction of the CD23/**nitric oxide** pathway in endothelial cells downregulates ICAM-1 expression and decreases cytoadherence of **Plasmodium** falciparum -infected erythrocytes
AUTHOR: Pino, P.; Vouldoukis, I.; Dugas, N.; Conti, M.; Nitcheu, J.; Traore, B.; Danis, M.; Dugas, B.; Mazier, D.
CORPORATE SOURCE: INSERM U511, Immunobiologie Cellulaire et Moleculaire des Infections Parasitaires, CHU Pitie-Salpetriere Paris VI, 75013 Paris, France.; E-mail: mazier@ext.jussieu.fr
SOURCE: Cellular Microbiology [Cell. Microbiol.], (20040900) vol. 6, no. 9, pp. 839-848.
ISSN: 1462-5814.
DOCUMENT TYPE: Journal
FILE SEGMENT: K
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Cytoadherence of parasitized red blood cells (PRBCs) to postcapillary venules and cytokine production are clearly involved in the pathogenesis of cerebral **malaria**. **Nitric oxide** and TNF-alpha have been proposed as major effector molecules both in protective and physiopathological processes during **malaria** infections. **Nitric oxide** production has been shown to be induced by engagement of CD23 antigen. This study aimed to investigate the potential role of the CD23/**nitric oxide** pathway in the control of the cytoadherence of PRBCs on human endothelial cells. We demonstrate

that normal human lung endothelial cells (HLECs) are able to express the low affinity receptor for IgE (Fc[isin]RII/CD23), following cell incubation with interleukin 4 or PRBCs. Ligation of the CD23 antigen by a specific anti-CD23 monoclonal antibody at the cell surface of HLECs was found to induce iNOS mRNA and protein expression, NO release and P. falciparum **killing**. In addition, the specific CD23-engagement on these cells also induced a significant decrease in ICAM-1 expression, an adhesion molecule implicated in PRBCs cytoadherence. These data not only described for the first time the expression of a CD23 antigen at the cell surface of endothelial cells but also suggest a possible new regulatory mechanisms via the CD23/NO pathway during **malaria** infection.

L62 ANSWER 3 OF 37 LIFESCI COPYRIGHT 2005 CSA on STN
ACCESSION NUMBER: 2004:32164 LIFESCI
TITLE: Mice Deficient in Interleukin-4 (IL-4) or IL-4 Receptor alpha Have Higher Resistance to Sporozoite Infection with **Plasmodium** berghei (ANKA) than Do Naive Wild-Type Mice
AUTHOR: Saeftel, M.*; Krueger, A.; Arriens, S.; Heussler, V.; Racz, P.; Fleischer, B.; Brombacher, F.; Hoerauf, A.
CORPORATE SOURCE: Institute for Medical Parasitology, Friedrich Wilhelm University Bonn, 53105 Bonn, Germany; E-mail: saeftel@bni.uni-hamburg.de
SOURCE: Infection and Immunity [Infect. Immun.], (20040100) vol. 72, no. 1, pp. 322-331.
ISSN: 0019-9567.
DOCUMENT TYPE: Journal
FILE SEGMENT: F; G; K
LANGUAGE: English
SUMMARY LANGUAGE: English
AB BALB/c interleukin-4 (IL-4 super(-/-)) or IL-4 receptor- alpha (IL-4r alpha super(-/-)) knockout (KO) mice were used to assess the roles of the IL-4 and IL-13 pathways during infections with the blood or liver stages of **plasmodium** in murine **malaria**. Intraperitoneal infection with the blood-stage erythrocytes of **Plasmodium** berghei (ANKA) resulted in 100% mortality within 24 days in BALB/c mice, as well as in the mutant mouse strains. However, when infected intravenously with the sporozoite liver stage, 60 to 80% of IL-4 super(-/-) and IL- 4r alpha super(-/-) mice survived, whereas all BALB/c mice succumbed with high parasitemia. Compared to infected BALB/c controls, the surviving KO mice showed increased NK cell numbers and expression of inducible **nitric oxide** synthase (iNOS) in the liver and were able to eliminate parasites early during infection. In vivo blockade of NO resulted in 100% mortality of sporozoite-infected KO mice. In vivo depletion of NK cells also resulted in 80 to 100% mortality, with a significant reduction in gamma interferon (IFN- gamma) production in the liver. These results suggest that IFN- gamma -producing NK cells are critical in host resistance against the sporozoite liver stage by inducing NO production, an effective **killing** effector molecule against **Plasmodium**. The absence of IL-4-mediated functions increases the protective innate immune mechanism identified above, which results in immunity against P. berghei infection in these mice, with no major role for IL-13.

L62 ANSWER 4 OF 37 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
DUPLICATE
ACCESSION NUMBER: 2003:37238702 BIOTECHNO
TITLE: Hemozoin increases IFN-γ-inducible macrophage **nitric oxide** generation through extracellular signal-regulated kinase- and NF-κB-dependent pathways
AUTHOR: Jaramillo M.; Gowda D.C.; Radzioch D.; Olivier M.
CORPORATE SOURCE: Dr. M. Olivier, Dept. of Microbiology and Immunology, McGill University, Duff Medical Building, 3775 University Street, Montreal, Que. H3A 2B4, Canada. E-mail: martin.olivier@staff.mcgill.ca
SOURCE: Journal of Immunology, (15 OCT 2003), 171/8 (4243-4253), 66 reference(s)

CODEN: JOIMA3 ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:37238702 BIOTECHNO
AB NO overproduction has been suggested to contribute to the immunopathology related to **malaria** infection. Even though a role for some parasite molecules (e.g., GPI) in NO induction has been proposed, the direct contribution of bemozoin (HZ), another parasite metabolite, remains to be established. Therefore, we were interested to determine whether **Plasmodium** falciparum (Pf) HZ and synthetic HZ, β-hematin, alone or in combination with IFN-γ, were able to induce macrophage (M.vphi.) NO synthesis. We observed that neither Pf HZ nor synthetic HZ led to NO generation in B10R murine M.vphi.; however, they significantly increased IFN-γ-mediated inducible NO synthase (iNOS) mRNA and protein expression, and NO production. Next, by investigating the transductional mechanisms involved in this cellular regulation, we established that HZ induces extracellular signal-regulated kinase (ERK)1/2 mitogen-activated protein kinase phosphorylation as well as NF-κB binding to the iNOS promoter, and enhances the IFN-γ-dependent activation of both second messengers. Of interest, cell pretreatment with specific inhibitors against either NF-κB or the ERK1/2 pathway blocked the HZ + IFN-γ-inducible NF-κB activity and significantly reduced the HZ-dependent increase on IFN-γ-mediated iNOS and NO induction. Even though selective **inhibition** of the Janus kinase 2/STAT1α pathway suppressed NO synthesis in response to HZ + IFN-γ, HZ alone did not activate this signaling pathway and did not have an up-regulating effect on the IFN-γ-induced Janus kinase 2/STAT1α phosphorylation and STAT1α binding to the iNOS promoter. In conclusion, our results suggest that HZ exerts a potent synergistic effect on the IFN-γ-inducible NO generation in M.vphi. via ERK- and NF-κB-dependent pathways.

L62 ANSWER 5 OF 37 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2003:36512848 BIOTECHNO
TITLE: Anti-adhesive effect of **nitric oxide** on **Plasmodium** falciparum cytoadherence under flow
AUTHOR: Serirom S.; Raharjo W.H.; Chotivanich K.; Loareesuwan S.; Kubes P.; Ho M.
CORPORATE SOURCE: Dr. M. Ho, Department of Microbiology, 3330 Hospital Dr NW, Calgary, Alta. T2N 4N1, Canada.
E-mail: mho@ucalgary.ca
SOURCE: American Journal of Pathology, (01 MAY 2003), 162/5 (1651-1660), 50 reference(s)
CODEN: AJPAA4 ISSN: 0002-9440
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:36512848 BIOTECHNO
AB **Nitric oxide** (NO) is widely known to inhibit platelet and leukocyte adhesion to endothelium through its regulatory effect on adhesion molecule expression. The objective of the present study was to investigate if NO affects the cytoadherence of **Plasmodium** falciparum-infected erythrocytes (IRBCs) to human microvascular endothelium (HDMECs) under flow conditions in vitro. The effect of endogenous NO was studied using the NO synthase inhibitor L-N.sup.G-nitroarginine-methyl-ester (L-NAME). **Treatment** of HDMECs with 3 mmol/L of L-NAME for 4 hours significantly enhanced IRBC adhesion and the effect could be reversed by an anti-P-selectin but not an anti-VCAM-1 antibody. The effect of exogenous NO on cytoadherence was studied by using the NO donor 3-(2-hydroxy-2-nitroso-1-propylhydrazino)-1-propanamine (PPN). PPN (300 μmol/L) **treatment** reduced the number of adherent IRBCs on resting HDMECs by down-regulating basal ICAM-1 expression, and on rumor necrosis factor-α-stimulated HDMECs

by **inhibition** of VCAM-1 induction and down-regulation of ICAM-1 expression. The inhibitory effect of PPN on rumor necrosis factorα-induced VCAM-1 expression at 24 hours was evident when the NO donor was added for as short as 2 hours. These findings suggest that NO may be protective against P. falciparum infection by inhibiting cytoad-herence, and underscore the therapeutic potential of NO in the **treatment** of severe falciparum **malaria**.

L62 ANSWER 6 OF 37 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 2003:37222438 BIOTECHNO
TITLE: Stromal cell-derived factor-1 production by spleen cells is affected by **nitric oxide** in protective immunity against blood-stage **Plasmodium** chabaudi CR in C57BL/6j mice
AUTHOR: Garnica M.R.; Silva J.S.; De Andrade Junior H.F.
CORPORATE SOURCE: H.F. De Andrade Junior, Lab. Protozoologia, Inst. de Med. Trop. de S. Paulo, Universidade de Sao Paulo, Av. Dr.E.C. Aguiar 470, 05403-000 Sao Paulo, SP, Brazil. E-mail: hfandrad@usp.br
SOURCE: Immunology Letters, (31 OCT 2003), 89/2-3 (133-142), 51 reference(s)
CODEN: IMLED6 ISSN: 0165-2478
DOCUMENT TYPE: Journal; Article
COUNTRY: Netherlands
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:37222438 BIOTECHNO
AB **Malaria**, a major endemic tropical disease, is caused by the infection of blood cells by **Plasmodium** protozoa. Most patients control their parasitemia by a not fully understood spleen-dependent mechanism. SDF-1α is a chemokine produced by stromal cells such as reticular spleen cells. **Nitric oxide** (NO) has several immune functions, including **killing** of intracellular pathogens and its function in **malaria** is debated. We have previously shown that SDF-1α production peaks during the ascending parasitemia in **Plasmodium** chabaudi infection and its supplementation in lethal models could reduce the parasitemia. In the present study, we analyzed SDF-1 production by spleen cells as related to NO metabolism in the P. chabaudi rodent **malaria** model using IFN-γ; TNFR and iNOS-knockout mice or iNOS-blocked, L-NAME- or aminoguanidine-treated mice. Parasitemia and production of SDF-1α and SDF-1β were determined by RT-PCR. In vitro NO production by spleen adherent cells was also tested. The data showed that parasitemia was less intense in both iNOS .sup.-.sup./.sup.- or NO-inhibited mice than in controls, with increased and long-lasting production of SDF-1α mRNA. In the absence of cytokines involved in the final regulation of NO production by effector cells, as is the case for TNFR.sup.-.sup./.sup.- and GKO mice, the infection progressed in an uncontrolled manner regardless of SDF-1α production, suggesting that these cytokines must be involved in the control of parasitemia after the SDF-1α dependent process. The SDF-1β isoform was constitutive in all experiments, with elevated levels only clearly seen in TNFR.sup.-.sup./.sup.- mice. We conclude that SDF-1 is involved in the promotion of parasitemia control in **malaria**, and excessive NO could affect its production.

L62 ANSWER 7 OF 37 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 2001:32187621 BIOTECHNO
TITLE: Interleukin-12- and gamma interferon-dependent protection against **malaria** conferred by CpG oligodeoxynucleotide in mice
AUTHOR: Gramzinski R.A.; Doolan D.L.; Sedegah M.; Davis H.L.; Krieg A.M.; Hoffman S.L.
CORPORATE SOURCE: S.L. Hoffman, Malaria Program, Naval Medical Research Center, 503 Robert Grant Ave., Silver Spring, MD 20910-7500, United States.

E-mail: hoffmans@nmrc.navy.mil
SOURCE: Infection and Immunity, (2001), 69/3 (1643-1649), 39 reference(s)
CODEN: INFIBR ISSN: 0019-9567
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2001:32187621 BIOTECHNO
AB Unmethylated CpG dinucleotides in bacterial DNA or synthetic oligodeoxynucleotides (ODNs) cause B-cell proliferation and immunoglobulin secretion, monocyte cytokine secretion, and activation of natural killer (NK) cell lyric activity and gamma interferon (IFN-γ) secretion in vivo and in vitro. The potent Th1-like immune activation by CpG ODNs suggests a possible utility for enhancing innate immunity against infectious pathogens. We therefore investigated whether the innate immune response could protect against **malaria**. **Treatment** of mice with CpG ODN 1826 (TCCATGACGTTCCTGACGTT, with the CpG dinucleotides underlined) or 1585 (ggGGTCAACGTTGAggggggG, with g representing diester linkages and phosphorothioate linkages being to the right of lowercase letters) in the absence of antigen 1 to 2 days prior to challenge with **Plasmodium** yoelii sporozoites conferred sterile protection against infection. A higher level of protection was consistently induced by CpG ODN 1826 compared with CpG ODN 1585. The protective effects of both CpG ODNs were dependent on interleukin-12, as well as IFN-γ. Moreover, CD8.sup.+ T cells (but not CD4.sup.+ T cells), NK cells, and **nitric oxide** were implicated in the CpG ODN 1585-induced protection. These data establish that the protective mechanism induced by administration of CpG ODN 1585 in the absence of parasite antigen is similar in nature to the mechanism induced by immunization with radiation-attenuated P. yoelii sporozoites or with plasmid DNA encoding preerythrocytic-stage P. yoelii antigens. We were unable to confirm whether CD8.sup.+ T cells, NK cells, or **nitric oxide** were required for the CpG ODN 1826-induced protection, but this may reflect differences in the potency of the ODNs rather than a real difference in the mechanism of action of the two ODNs. This is the first report that stimulation of the innate immune system by CpG immunostimulatory motifs can confer sterile protection against **malaria**.

L62 ANSWER 8 OF 37 LIFESCI COPYRIGHT 2005 CSA on STN
ACCESSION NUMBER: 2001:87046 LIFESCI
TITLE: Regulatory Interactions between Iron and **Nitric Oxide** Metabolism for Immune Defense against **Plasmodium** falciparum Infection
AUTHOR: Fritsche, G.; Larcher, C.; Schennach, H.; Weiss, G.
CORPORATE SOURCE: Department of Internal Medicine, University Hospital, Innsbruck, Austria
SOURCE: Journal of Infectious Diseases [J. Infect. Dis.], (20010501) vol. 183, no. 9, pp. 1388-1394.
ISSN: 0022-1899.
DOCUMENT TYPE: Journal
FILE SEGMENT: K
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Iron chelation therapy of **Plasmodium** falciparum infection alleviates the clinical course of cerebral **malaria** in children. This study assessed the underlying mechanisms of this therapy. Cytokine stimulation of human (intestinal cell line DLD-1) or murine cells (murine macrophage cell line RAW 264.7) resulted in increased **nitric oxide** (NO) formation and decreased survival of **plasmodia** within cocultured human erythrocytes. The addition of desferrioxamine (DFO) before cytokine **treatment** increased both NO formation and parasite **killing** but had no effect in the presence of the inhibitor of NO formation, L-N6-(1-iminoethyl)-lysine. Moreover, peroxynitrite, which is formed after chemical reaction of NO with superoxide, appears to be the principal effector molecule for macrophage-mediated cytotoxicity toward P. falciparum, and interferon-

gamma is a major regulatory cytokine for this process. The effect of DFO on the clearance of **plasmodia** appears to be due to enhanced generation of NO, rather than to limitation of iron availability to the parasite.

L62 ANSWER 9 OF 37 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001:32096481 BIOTECHNO
TITLE: Cerebral **malaria** in mice: Interleukin-2 **treatment** induces accumulation of γδ T cells in the brain and alters resistant mice to susceptible-like phenotype
AUTHOR: Haque A.; Echchannaoui H.; Seguin R.; Schwartzman J.; Kasper L.H.; Haque S.
CORPORATE SOURCE: Dr. A. Haque, INSERM U399, Faculte de Medecine, Universite de la Mediterranee, 27 Bvd. Jean Moulin, 13385 Marseille, France.
E-mail: h.azizul@medecine.univ-mrs.fr
SOURCE: American Journal of Pathology, (2001), 158/1 (163-172), 47 reference(s)
CODEN: AJPAA4 ISSN: 0002-9440
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2001:32096481 BIOTECHNO
AB In this study, we report that infection with **Plasmodium** yoelii 17XL, a lethal strain of rodent **malaria**, does not result in death in the DBA/2 strain of mice. In contrast to BALB/c mice, DBA/2 mice developed significantly less parasitemia and never manifested symptoms of cerebral **malaria** (CM) on infection with this parasite. Moreover, the histological changes evident in the brain of susceptible BALB/c were absent in DBA/2 mice. Interestingly, the resistant DBA/2 mice when treated with recombinant interleukin (IL)-2, were found to develop CM symptoms and the infection became fatal by 6 to 8 days after infection. This condition was associated with an augmented interferon-γ and **nitric oxide** production. Unexpectedly, IL-10 levels were also elevated in IL-2-treated DBA/2 mice during late stage of infection (at day 6 of infection) whereas the inverse relationship between IL-10 and interferon-γ or **nitric oxide** was maintained in the file early stage of infection (at day 3 after infection). The level of tumor necrosis factor-α production was moderately increased in the late phase of infection in these mice. Histology of brain from IL-2-treated mice demonstrated the presence of parasitized erythrocytes and infiltration of lymphocytes in cerebral vessels, and also displayed some signs of endothelial degeneration. Confocal microscopical studies demonstrated preferential accumulation of γδ T cells in the cerebral vessels of IL-2-treated and -infected mice but not in mice treated with IL-2 alone. The cells recruited in the brain were activated because they demonstrated expression of CD25 (IL-2R) and CD54 (intercellular adhesion molecule 1) molecules. Administration of anti-γδ mAb prevented development of CM in IL-2-treated mice until day 18 after infection whereas mice treated with control antibody showed CM symptoms by day 6 after infection. The information concerning creating pathological sequelae and death in an otherwise resistant mouse strain provides an interesting focus for the burden of pathological attributes on death in an infectious disease.

L62 ANSWER 10 OF 37 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
DUPLICATE
ACCESSION NUMBER: 2000:30728188 BIOTECHNO
TITLE: **Nitric oxide** is neither necessary nor sufficient for resolution of **Plasmodium** chabaudi **malaria** in mice
AUTHOR: Van der Heyde H.C.; Gu Y.; Zhang Q.; Sun G.; Grisham M.B.
CORPORATE SOURCE: Dr. H.C. Van der Heyde, Dept. of Microbiol. and Immunology, Louisiana St. Univ. Hlth. Sci. Ctr., P.O.

Box 33932, Shreveport, LA 71130, United States.
E-mail: hvande@lsumc.edu
SOURCE: Journal of Immunology, (15 SEP 2000), 165/6 (3317-3323), 42 reference(s)
CODEN: JOIMA3 ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2000:30728188 BIOTECHNO
AB **Malaria** is a life-threatening re-emerging disease, yet it is still not clear how bloodstage malarial parasites are killed. **Nitric oxide** (NO), which has potent anti-microbial activity, may represent an important **killing** mechanism. The production of NO during descending **Plasmodium** chabaudi parasitemia, a period when parasites are killed by the immune response, supports this concept. However, NOS2(0/0) and NOS3(0/0) mice as well as mice treated with NO synthase 2 (NOS2) inhibitors do not develop exacerbated **malaria**, indicating that NO production is not necessary for the suppression of P. chabaudi parasitemia. It is possible due to the plasticity in the immune response during **malaria** that Ab-mediated immunity is enhanced in the absence of NO, thereby explaining the lack of exacerbated **malaria** in NOS-deficient mice even though NO may function in protection. However, NOS2- and B cell-deficient mice, which cannot use Ab-mediated immunity, suppress their parasitemia with a similar time course as B cell-deficient controls. C57BL/6 mice treated with Propionibacterium acnes to elicit high levels of macrophage-derived NO have a similar time course of P. chabaudi parasitemia as P. acnes-treated NOS2(0/0) mice, which do not produce NO; this indicates that NO is not sufficient for parasite **killing**. Collectively, these results indicate that NO is not necessary or sufficient to resolve P. chabaudi **malaria**.

L62 ANSWER 11 OF 37 LIFESCI COPYRIGHT 2005 CSA on STN
ACCESSION NUMBER: 2001:101228 LIFESCI
TITLE: **Nitric Oxide** Inhibits Falcipain, the **Plasmodium** falciparum Trophozoite Cysteine Protease
AUTHOR: Venturini, G.; Colasanti, M.; Salvati, L.; Gradoni, L.; Ascenzi, P.*
CORPORATE SOURCE: Dipartimento di Biologia, Universita di Roma "Tre,', Viale Guglielmo Marconi 446, I-00146, Rome, Italy; E-mail: ascenzi@bio.uniroma3.it
SOURCE: Biochemical and Biophysical Research Communications [Biochem. Biophys. Res. Commun.], (20000107) vol. 267, no. 1, pp. 190-193.
ISSN: 0006-291X.
DOCUMENT TYPE: Journal
FILE SEGMENT: K
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Nitric oxide** (NO) is a pluripotent regulatory molecule possessing, among others, an antiparasitic activity. In the present study, the inhibitory effect of NO on the catalytic activity of falcipain, the papain-like cysteine protease involved in **Plasmodium** falciparum trophozoite hemoglobin degradation, is reported. In particular, NO donors S-nitrosoglutathione (GSNO), (plus or minus)-(E)-4-ethyl-2-[(E)-hydroxyimino]-5-nitro-3-hexenamide (NOR-3), 3-morpholinosydnonimine (SIN-1), and sodium nitroprusside (SNP) inhibit dose-dependently the falcipain activity present in the P. falciparum trophozoite extract, this effect likely attributable to S-nitrosylation of the Cys25 catalytic residue. The results represent a new insight into the modulation mechanism of falcipain activity, thereby being relevant in developing new strategies for **inhibition** of the P. falciparum life cycle. Copyright 2000 Academic Press.

L62 ANSWER 12 OF 37 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1999:29314455 BIOTECHNO
TITLE: Immunization with heat-killed Toxoplasma gondii

stimulates an early IFN- γ response and induces protection against virulent murine **malaria**

AUTHOR: Haque A.; Graille M.; Kasper L.H.; Haque S.

CORPORATE SOURCE: A. Haque, Immunol./Genet. Maladies Parasit., INSERM U399, Faculte de Medecine, La Timone, 13385 Marseille, France.
E-mail: haque@club-internet.fr

SOURCE: Vaccine, (04 JUN 1999), 17/20-21 (2604-2611), 32 reference(s)
CODEN: VACCDE ISSN: 0264-410X

PUBLISHER ITEM IDENT.: S0264410X9900050X

DOCUMENT TYPE: Journal; Article

COUNTRY: United Kingdom

LANGUAGE: English

SUMMARY LANGUAGE: English

AN 1999:29314455 BIOTECHNO

AB In this study, we describe protection of BALB/c mice by immunization with heat-killed T. gondii tachyzoites against infection with **Plasmodium** yoelii 17XL which causes cerebral **malaria** and death in mice by day 7-8 post infection. Immunization resulted significant reduction in parasitemia at the peak period of infection. Protection induced by heat-killed T. gondii was associated with marked increase in NK cell number and IFN-γ mRNA expression early in the infection. The level of IFN-γ or TNF-α was found to diminish in T. gondii-treated mice as the infection progressed to the late stage. This declined response of IFN-γ or TNF-α was associated with marked increase in the expression of IL-10, a counterregulatory cytokine. Pretreatment of mice with live T. gondii induced poor level of protection as compared with that of heat-killed parasites. Mice that received P. yoelii infection alone, had an elevated IFN-γ response in the late stage of infection. Development of cerebral **malaria** in untreated mice was accompanied by an augmented production of TNF-α and **nitric oxide** (NO), the proinflammatory mediators. These findings suggest that nonspecific immunization with T. gondii leads to restoration of an early IFN-γ response in P. yoelii-infected mice and in the establishment of an immunoregulatory mechanism that effectively antagonizes the disease-promoting effects of proinflammatory cytokines in the late phase of infection.

L62 ANSWER 13 OF 37 LIFESCI COPYRIGHT 2005 CSA on STN

ACCESSION NUMBER: 1999:73232 LIFESCI

TITLE: Gamma interferon production is critical for protective immunity to infection with blood-stage **Plasmodium** berghei XAT but neither NO production nor NK cell activation is critical

AUTHOR: Yoneto, T.; Yoshimoto, T.; Wang, Ch.-R.; Takahama, Y.; Tsuji, M.; Waki, S.; Nariuchi, H.*

CORPORATE SOURCE: Department of Allergology, Institute of Medical Science, The University of Tokyo, 4-6-1 Shirokamedai, Minato-ku, Tokyo 108-8639 Japan; E-mail: hnari@hgc.ims.u-tokyo.ac.jp

SOURCE: Infection and Immunity [Infect. Immun.], (19990500) vol. 65, no. 5, pp. 2349-2356.
ISSN: 0019-9567.

DOCUMENT TYPE: Journal

FILE SEGMENT: K; F

LANGUAGE: English

SUMMARY LANGUAGE: English

AB We have examined the roles of gamma interferon (IFN- gamma), **nitric oxide** (NO), and natural killer (NK) cells in the host resistance to infection with the blood-stage malarial parasite **Plasmodium** berghei XAT, an irradiation-induced attenuated variant of the lethal strain P. berghei NK65. Although the infection with P. berghei XAT enhanced NK cell lytic activity of splenocytes, depletion of NK1.1 super(+) cells caused by the **treatment** of mice with anti-NK1.1 antibody affected neither parasitemia nor IFN- gamma production by their splenocytes. The P. berghei XAT infection induced a large amount of NO production by splenocytes during the first peak of parasitemia, while P. berghei NK65 infection induced a small amount. Unexpectedly,

however, mice deficient in inducible **nitric oxide** synthase (iNOS super(-/-)) cleared P. berghei XAT after two peaks of parasitemia were observed, as occurred for wild-type control mice. Although the infected (iNOS super(-/-)) mouse splenocytes did not produce a detectable level of NO, they produced an amount of IFN- gamma comparable to that produced by wild-type control mouse splenocytes, and **treatment** of these mice with neutralizing anti-IFN- gamma antibody led to the progression of parasitemia and fatal outcome. CD4 super(-/-) mice infected with P. berghei XAT could not clear the parasite, and all these mice died with apparently reduced IFN- gamma production. Furthermore, **treatment** with carrageenan increased the susceptibility of mice to P. berghei XAT infection. These results suggest that neither NO production nor NK cell activation is critical for the resistance to P. berghei XAT infection and that IFN- gamma plays an important role in the elimination of malarial parasites, possibly by the enhancement of phagocytic activity of macrophages.

L62 ANSWER 14 OF 37 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1999:29200482 BIOTECHNO
TITLE: Altered immune response of interferon regulatory factor 1-deficient mice against **Plasmodium** berghei blood-stage **malaria** infection
AUTHOR: Tan R.S.-P.; Feng C.; Asano Y.; Kara A.U.
CORPORATE SOURCE: A.U. Kara, Molecular Parasitology Laboratory, Department of Biological Sciences, National University of Singapore, 10 Kent Ridge Crescent, Singapore 119260, Singapore.
E-mail: dbsauk@leonis.nus.edu.sg
SOURCE: Infection and Immunity, (1999), 67/5 (2277-2283), 47 reference(s)
CODEN: INFIBR ISSN: 0019-9567
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1999:29200482 BIOTECHNO
AB **Nitric oxide** (NO) is a short-lived biological mediator which can be induced in various cell types and is able to cause many metabolic changes in target cells. **Inhibition** of tumor cell growth and antimicrobial activity has been attributed to the stimulation of NO production by transcriptional upregulation of inducible **nitric oxide** synthase. In the present study, we used mice devoid of functional interferon regulatory factor 1 by targeted gene disruption (IRF-1(-/-) to investigate the role of NO in the host immune response against blood-stage **Plasmodium** berghei ANKA infection. IRF-1(-/-) mice survived longer with a later onset of and a lower peak parasitemia despite the inability to produce appreciable levels of NO. The administration of exogenous interleukin-12 (IL-12) was able to prolong survival in the wild- type mice with an upregulation in the expression of both gamma interferon (IFN-γ) and NO. However, the administration of IL-12 did not improve the survival of IRF-1(-/-) mice. These studies indicate that while IL-12 is able to mediate protection via an IFN-γ- and NO-dependent pathway in the wild- type mice, such a protective mechanism may not be functional in the IRF-1(- /-) mice. Our results suggest that NO may not be essential for host immunity to the parasite and that IRF-1(-/-) mice are able to induce an IFN-γ- and NO-independent mechanism against P. berghei infection.

L62 ANSWER 15 OF 37 LIFESCI COPYRIGHT 2005 CSA on STN
ACCESSION NUMBER: 1999:73247 LIFESCI
TITLE: Altered immune response of interferon regulatory factor 1-deficient mice against **Plasmodium** berghei blood-stage **malaria** infection
AUTHOR: Tan, R.S.-P.; Feng, Ch.; Asano, Y.; Kara, A.U.*
CORPORATE SOURCE: Molecular Parasitology Laboratory, Department of Biological Sciences, National University of Singapore, 10 Kent Ridge Crescent, Singapore 119260, Singapore,; E-mail: dbsauk@leonis.nus.edu.sg

SOURCE: Infection and Immunity [Infect. Immun.], (19990500) vol. 65, no. 5, pp. 2277-2283.
ISSN: 0019-9567.
DOCUMENT TYPE: Journal
FILE SEGMENT: K; F
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Nitric oxide** (NO) is a short-lived biological mediator which can be induced in various cell types and is able to cause many metabolic changes in target cells. **Inhibition** of tumor cell growth and antimicrobial activity has been attributed to the stimulation of NO production by transcriptional upregulation of inducible **nitric oxide** synthase. In the present study, we used mice devoid of functional interferon regulatory factor 1 by targeted gene disruption (IRF-1 super(-/-)) to investigate the role of NO in the host immune response against blood-stage **Plasmodium** berghei ANKA infection. IRF-1 super(-/-) mice survived longer with a later onset of and a lower peak parasitemia despite the inability to produce appreciable levels of NO. The administration of exogenous interleukin-12 (IL-12) was able to prolong survival in the wild-type mice with an upregulation in the expression of both gamma interferon (IFN- gamma) and NO. However, the administration of IL-12 did not improve the survival of IRF-1 super(-/-) mice. These studies indicate that while IL-12 is able to mediate protection via an IFN- gamma - and NO-dependent pathway in the wild-type mice, such a protective mechanism may not be functional in the IRF-1 super(-/-) mice. Our results suggest that NO may not be essential for host immunity to the parasite and that IRF-1 super(-/-) mice are able to induce an IFN- gamma - and NO-independent mechanism against P. berghei infection.

L62 ANSWER 16 OF 37 LIFESCI COPYRIGHT 2005 CSA on STN
ACCESSION NUMBER: 1999:82697 LIFESCI
TITLE: **Malaria** parasite-specific Th1-like T cells simultaneously reduce parasitemia and promote disease
AUTHOR: Hirunpetcharat, C.; Finkelman, F.; Clark, I.A.; Good, M.F.*
CORPORATE SOURCE: Queensland Institute of Medical Research, Royal Brisbane Hospital, Brisbane 4029, Australia
SOURCE: Parasite Immunology [Parasite Immunol.], (19990600) vol. 21, no. 6, pp. 319-329.
ISSN: 0141-9838.
DOCUMENT TYPE: Journal
FILE SEGMENT: F; K
LANGUAGE: English
SUMMARY LANGUAGE: English

AB CD4 super(+) T cells have been implicated in immunity to the blood stages of **malaria** and cytokines associated with both monocyte and T cell activation have been implicated in disease. To determine whether specific T cells capable of inhibiting parasite growth can also mediate pathology we have transfused populations of **Plasmodium** berghei-specific T cells into normal and immunodeficient naive mice. We observed that they could inhibit parasite growth but were unable to save the animals which exhibited significantly greater anaemia and weight loss than control infected animals receiving either no T cells or T cells specific for ovalbumin. T cell-dependent tumour necrosis factor (TNF) alpha was a critical component in both parasite **killing** and disease promotion. Experiments with blocking antibodies demonstrated that all T-cell mediated antiparasitic immunity and all T-cell mediated weight loss was TNF-dependent. Blocking TNF- alpha in mice that received parasite-specific T cells prolonged the survival of the mice. Nitic oxide demonstrated no antiparasite effect, but was involved in the regulation of T-cell mediated weight loss. The data thus show that while parasite-specific CD4 super(+) T cells can significantly limit parasite growth, such an effect need not be beneficial to the host, and that TNF-alpha and **nitric oxide** are critical effector molecules operating downstream of parasite-specific T cells in both immunity and disease.

L62 ANSWER 17 OF 37 AGRICOLA Compiled and distributed by the National Agricultural Library of the Department of Agriculture of the United States

 DUPLICATE 5
ACCESSION NUMBER: 2000:48404 AGRICOLA
DOCUMENT NUMBER: IND22056341
TITLE: Modulation of host immune responses by protozoal DNA.
AUTHOR(S): Brown, W.C.; Suarez, C.E.; Shoda, L.K.M.; Estes, D.M.
CORPORATE SOURCE: Washington State University, Pullman, WA.
AVAILABILITY: DNAL (SF757.2.V38)
SOURCE: Veterinary immunology and immunopathology, Dec 15, 1999. Vol. 72, No. 1/2. p. 87-94
Publisher: Amsterdam : Elsevier.
CODEN: VIIMDS; ISSN: 0165-2427
NOTE: Paper presented at the "5th International Veterinary Immunology Symposium," Nov. 8-13, 1998, Ludhiana, India.
Includes references
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Article
FILE SEGMENT: Non-U.S. Imprint other than FAO
LANGUAGE: English
AB The pathology caused by acute Babesia bovis infection is similar to that seen in severe human **malaria** caused by **Plasmodium** falciparum infection, which is related to dysregulated production of inflammatory cytokines and **nitric oxide** (NO). We have observed induction of NO, inducible **nitric oxide** synthase (iNOS) and inflammatory cytokines in macrophages by B. bovis. Furthermore, proliferation of lymphocytes from individuals never exposed to certain protozoal pathogens can be induced by crude protozoal parasite extracts. We have repeatedly observed stimulation of naive PBMC from cattle to antigenic extracts of Babesia bovis. Based on recent studies demonstrating the mitogenicity of bacterial and other non-vertebrate DNAs for murine B cells and macrophages, the mitogenic properties of B. bovis DNA were examined. B. bovis and E. coli DNAs induced proliferation of PBMC and purified B cells from non-exposed cattle. Stimulatory activity was reduced by DNase **treatment** and methylation with CpG methylase, indicating the presence of stimulatory non-methylated CpG motifs in the B. bovis genome. B. bovis and E. coli DNAs enhanced IgG secretion by cultured B cells, stimulating IgG1 and more strongly, IgG2. Several hexameric CpG immunostimulatory sequences (ISS) active for murine B cells were identified in an 11 kb fragment of B. bovis DNA. An oligodeoxyribonucleotide containing one of these (AACGTT), located in the rhoptry associated protein-1 (rap-1) open reading frame, stimulated B cell proliferation. These studies identify a potential mechanism by which protozoal parasites may modulate host immune responses, leading to consequences such as hypergammaglobulinemia and splenomegaly. These results also support the use of ISS as vaccine adjuvants to enhance Type 1 immune responses in cattle.

L62 ANSWER 18 OF 37 BIOTECHNO
DUPLICATE
ACCESSION NUMBER: 1999:29143428 BIOTECHNO
TITLE: A dichotomous role for **nitric oxide** in protection against blood stage **malaria** infection
AUTHOR: Taylor-Robinson A.W.; Smith E.C.
CORPORATE SOURCE: A.W. Taylor-Robinson, Department of Biology, University of Leeds, Clarendon Way, Leeds LS2 9JT, United Kingdom.
E-mail: bgyawtr@leeds.ac.uk
SOURCE: Immunology Letters, (15 MAR 1999), 67/1 (1-9), 40 reference(s)
CODEN: IMLED6 ISSN: 0165-2478
PUBLISHER ITEM IDENT.: S0165247898001485
DOCUMENT TYPE: Journal; Article
COUNTRY: Netherlands
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1999:29143428 BIOTECHNO

AB **Nitric oxide** (NO) is cytotoxic and cytostatic to blood stage **malaria** parasites in vitro, but the precise mechanism(s) by which it mediates an effect in vivo is not known. In particular, whether or not control of acute parasitemia depends on the presence of NO is unclear. We have shown previously that blocking NO synthesis at the time of its induction may cause an increase in peak primary parasitemia during infection of mice with **Plasmodium** chabaudi, suggesting that NO may be parasiticidal in vivo. However, as recent data indicate that NO suppresses Th1 cell proliferation in vitro by downregulating IL-2 production, we have investigated whether this immunoregulatory function of NO affects its capacity for anti-malarial activity. **Treatment** of P. chabaudi-infected mice with the iNOS inhibitor aminoguanidine hemisulfate (AG) starting just prior to the peak of primary parasitemia caused a significant elevation and extension of the acute infection and led to a partial but significant abrogation of the suppression of spleen cell proliferation to both mitogen and specific antigen observed when NO synthesis was not blocked. In the absence of NO, levels of IL-2, but not of IFN-γ, TNF-α, or of any Th2-regulated cytokines examined, increased significantly. However, when AG **treatment** was brought forward to the early ascending phase of primary parasitemia, significantly increased levels of IFN-γ and TNF-α, as well as of IL-2, were observed over those for infected control mice similarly treated with phosphate-buffered saline. Moreover, despite the absence of NO, parasitemias of AG-treated mice were not significantly elevated. The effect of AG therefore appeared to be dependent upon the timing of its administration in vivo. We propose that during **malaria** infections, there is a dynamic balance between the regulatory and anti- parasitic roles of NO. While the immunosuppressive function of NO leads to a downregulation in vivo of production of IL-2, and indirectly of IFN-γ and TNF-α, this perceived weakening of the host cell-mediated immune response is in part masked by the protective anti-malarial effects of NO itself.

L62 ANSWER 19 OF 37 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1998:28224159 BIOTECHNO
TITLE: The mosquito Anopheles stephensi limits **malaria** parasite development with inducible synthesis of **nitric oxide**
AUTHOR: Luckhart S.; Vodovotz Y.; Cui L.; Rosenberg R.
CORPORATE SOURCE: S. Luckhart, Department of Biochemistry, 111 Engel Hall, Virginia Tech, Blacksburg, VA 24061, United States.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (12 MAY 1998), 95/10 (5700-5705), 41 reference(s)
CODEN: PNASA6 ISSN: 0027-8424
DOCUMENT TYPE: Journal; Conference Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1998:28224159 BIOTECHNO
AB We have discovered that the mosquito Anopheles stephensi, a natural vector of human **malaria**, limits parasite development with inducible synthesis of **nitric oxide** (NO). Elevated expression of A. stephensi NO synthase (NOS), which is highly homologous to characterized NOS genes, was detected in the midgut and carcass soon after invasion of the midgut by **Plasmodium**. Early induction is likely primed by bacterial growth in the blood meal. Later increases in A. stephensi NOS expression and enzyme activity occurred at the beginning of sporozoite release. Circulating levels of nitrite/nitrate, end-products of NO synthesis, were significantly higher in **Plasmodium** -infected mosquitoes. Dietary provision of the NOS substrate L-arginine reduced **Plasmodium** infections in A. stephensi. In contrast, dietary provision of a NOS inhibitor significantly increased parasite numbers in infected mosquitoes, confirming that A. stephensi limits **Plasmodium** development with NO.

L62 ANSWER 20 OF 37 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN

DUPLICATE
ACCESSION NUMBER: 1998:28267842 BIOTECHNO
TITLE: A pathogenic role of IL-12 in blood-stage murine **malaria** lethal strain **Plasmodium** berghei NK65 infection
AUTHOR: Yoshimoto T.; Takahama Y.; Wang C.-R.; Yoneto T.; Waki S.; Nariuchi H.
CORPORATE SOURCE: Dr. T. Yoshimoto, Department of Allergology, Institute of Medical Science, University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo 108-8639, Japan.
SOURCE: Journal of Immunology, (01 JUN 1998), 160/11 (5500-5505), 55 reference(s)
CODEN: JOIMA3 ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1998:28267842 BIOTECHNO
AB We studied whether the infection with a blood-stage murine **malaria** lethal **Plasmodium** berghei NK65 induces IL-12 production, and if so, how the IL-12 production is involved in the protection or pathogenesis. The infection of C57BL/6 mice enhanced mRNA expression of IL-12 p40 and also IFN-γ, IL-4, and IL-10 in both spleen and liver during the early course of the infection. It also enhanced the mRNA expression of TNF-α, Fas ligand, and cytokine-inducible **nitric oxide** synthase. Increased IL-12 p40 production was also observed in the culture supernatant of spleen cells and in sera of infected mice. In addition, the infection caused massive liver injury with elevated serum glutamic-oxaloacetic transaminase and serum glutamic-pyruvic transaminase activities and body weight loss. **Treatment** of these infected mice with neutralizing mAb against IL-12 prolonged the survival and diminished the liver injury with reduced elevation of serum serum glutamic- oxaloacetic transaminase and serum glutamic-pyruvic transaminase activities and decreased body weight loss. However, the anti-IL-12 **treatment** did not affect parasitemia, and all these mice eventually died. Similar results were obtained when infected mice were treated with neutralizing mAb against IFN- γ. Moreover, anti-IL-12 **treatment** greatly reduced the secretion and mRNA expression of IFN-γ in both spleen and liver. These results suggest that the lethal P. berghei NK65 infection induces IL-12 production and that the IL-12 is involved in the pathogenesis of liver injury via IFN-γ production rather than the protection.

L62 ANSWER 21 OF 37 BIOTECHNO COPYRIGHT 2005 Elsevier Science B.V. on STN
DUPLICATE
ACCESSION NUMBER: 1998:28243594 BIOTECHNO
TITLE: Interleukin-12-dependent mechanisms in the clearance of blood-stage murine **malaria** parasite **Plasmodium** berghei XAT, an attenuated variant of P. berghei NK65
AUTHOR: Yoshimoto T.; Yoneto T.; Waki S.; Nariuchi H.
CORPORATE SOURCE: Dr. T. Yoshimoto, Dept. of Allergology, Institute of Medical Science, University of Tokyo, 4-6-1 Shirokanedai, Minatoku, Tokyo 108-8639, Japan.
E-mail: yoshimot@ims.u-tokyo.ac.jp
SOURCE: Journal of Infectious Diseases, (1998), 177/6 (1674-1681), 43 reference(s)
CODEN: JIDIAQ ISSN: 0022-1899
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1998:28243594 BIOTECHNO
AB The mechanism of development of host resistance to blood-stage malarial infection was studied by use of an irradiation-induced attenuated variant, **Plasmodium** berghei XAT, obtained from a lethal strain, P. berghei NK65. The infection enhanced mRNA expression of interleukin (IL)-12 p40 and also of interferon (IFN)-γ, IL-4, IL-10, and